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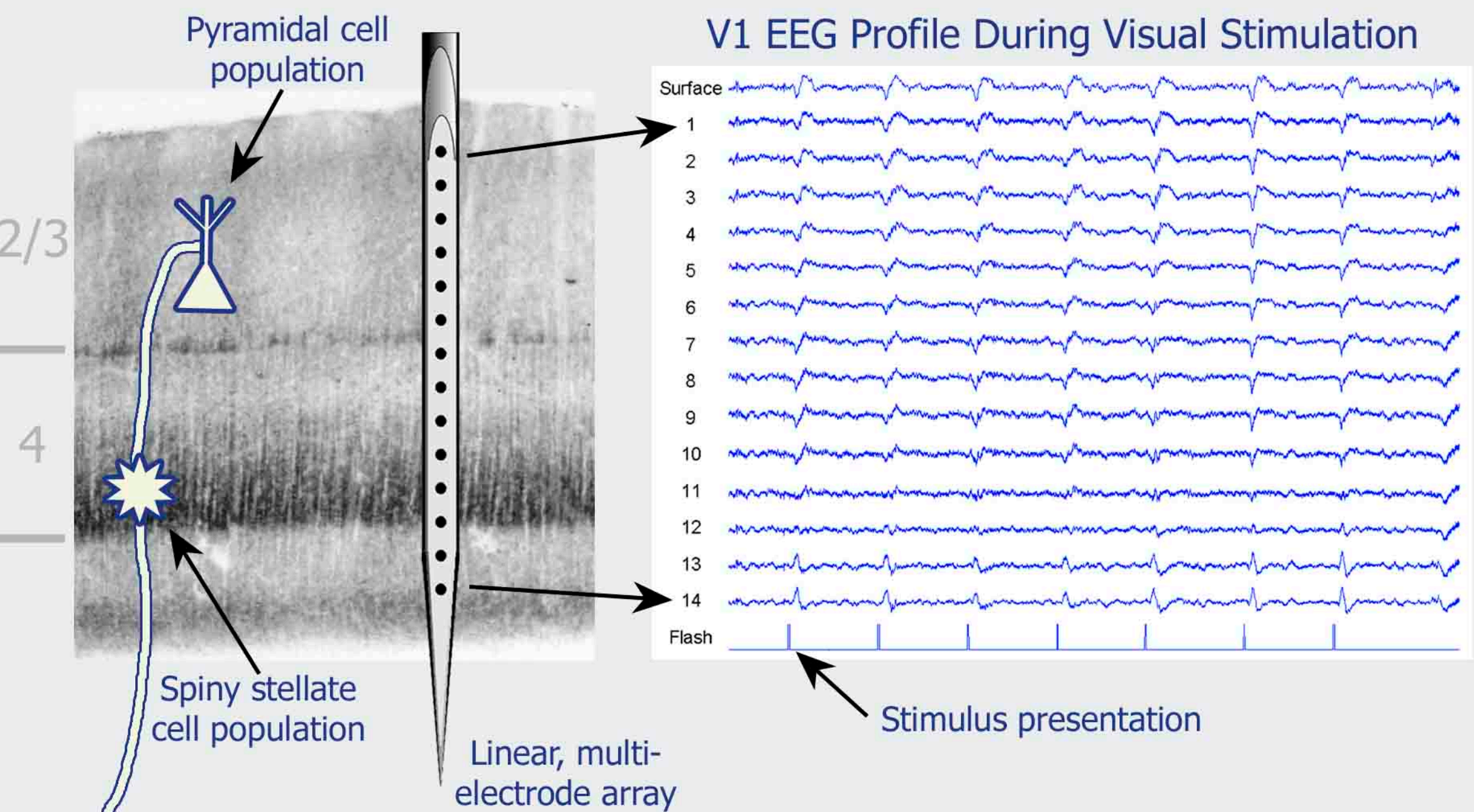
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## Abstract

Accurate characterization of single-trial field potential responses is critical from a number of perspectives. For example, it allows differentiation of an evoked response from ongoing EEG. We previously developed the multiple component Event Related Potential (mcERP) algorithm to improve resolution of the single-trial evoked response. The mcERP model states that multiple components, each specified by a stereotypic waveform varying in latency and amplitude from trial to trial, comprise the evoked response. Application of the mcERP algorithm to simulated data with three independent, synthetic components has shown that the model is capable of separating these components and estimating their variability. Application of the model to single-trial, visual evoked potentials recorded simultaneously from all V1 laminae in an awake, fixating macaque yielded local and far-field components. Certain local components estimated by the model were distributed in both granular and supragranular laminae. This suggests a linear coupling between the responses of thalamo-recipient neuronal ensembles and subsequent responses of supragranular neuronal ensembles, as predicted by the feedforward anatomy of V1. Our results indicate that the mcERP algorithm provides a valid estimation of single-trial responses. This will enable analyses that depend on trial-to-trial variations and those that require separation of the evoked response from background EEG rhythms.

## Why Single Trials?

A sensory stimulus activates multiple neuronal ensembles whose electrical activity can be measured. Activation of these ensembles exhibits trial-to-trial variability, which when characterized reveals a "higher resolution picture" of sensory processing schema. For example, the V1 feedforward circuit model states that visual input enters layer 4C at a precise latency and progresses to layers 2/3. Trial-to-trial co-variation in activity from these two layers is thus expected. Deviations in onset latency and amplitude might signal multiple activation states related to different task or subject conditions. Variability in single-trial evoked responses also prohibits accurate separation of stimulus-evoked activity from ongoing EEG rhythms. Thus single-trial dynamics must be characterized and studied to understand processing.



## References

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## The mcERP Model

The mcERP model defines multiple components as stereotypical waveshapes that may vary in amplitude and latency from trial to trial. This is expressed mathematically as:

$$x_{mr}(t) = \sum_{n=1}^N C_{mn} \alpha_{nr} s_n(t - \tau_{nr}) + \eta_{mr}(t)$$

Waveshape of the  $n^{\text{th}}$  component

Recorded signal in the  $m^{\text{th}}$  electrode channel during the  $r^{\text{th}}$  trial

Unpredictable signal in the  $m^{\text{th}}$  electrode channel during the  $r^{\text{th}}$  trial

Coupling between the  $n^{\text{th}}$  component and  $m^{\text{th}}$  electrode channel

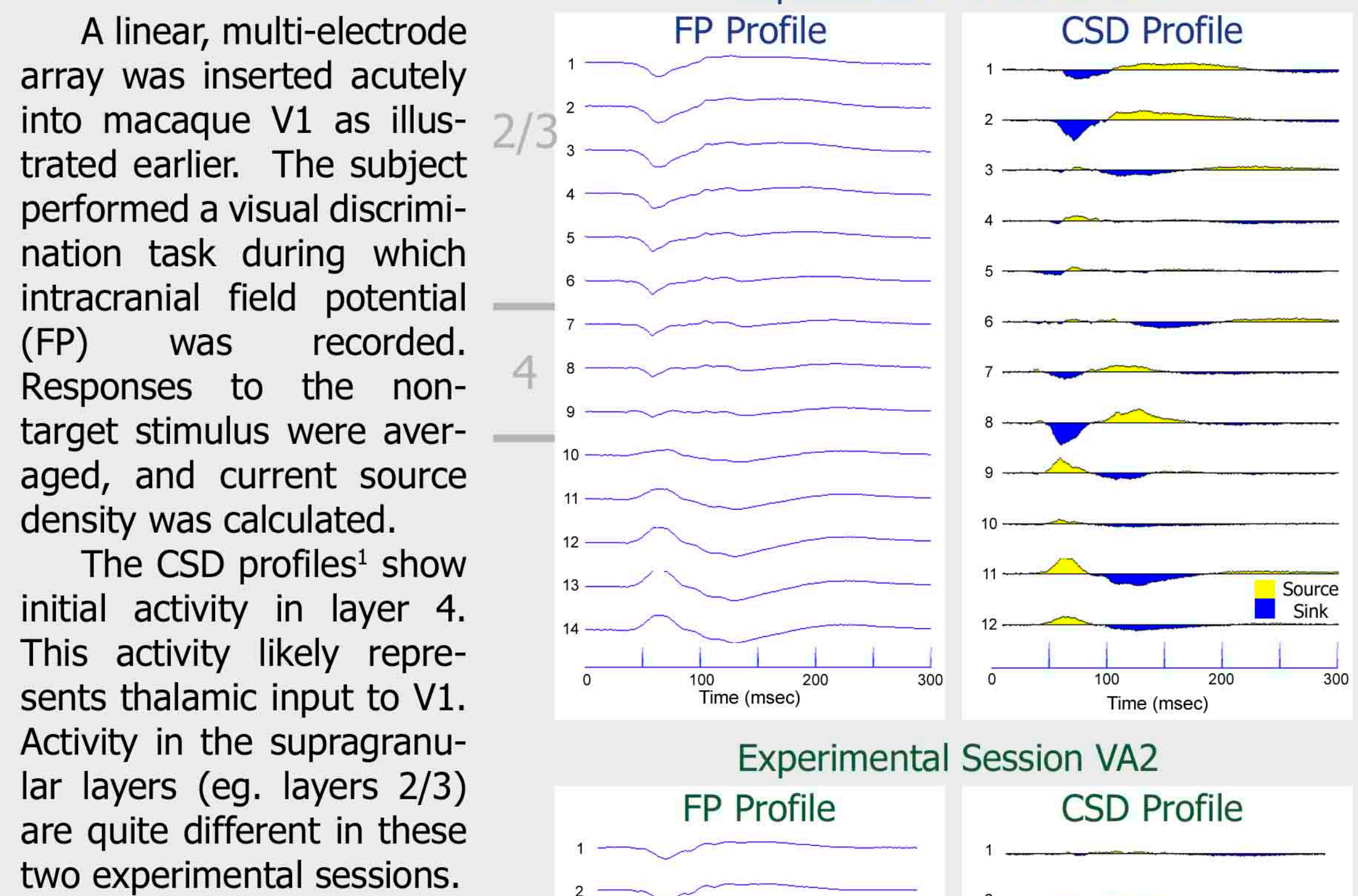
Amplitude scaling for the  $n^{\text{th}}$  component in the  $r^{\text{th}}$  trial

Latency shift of the  $n^{\text{th}}$  component in the  $r^{\text{th}}$  trial

Index Legend	
$m$	electrode channel
$r$	trial
$t$	time
$n$	component
$N$	total components

Bayes' theorem is applied to compute the posterior probability of the model from which *maximum a posteriori* (MAP) solutions are estimated using a fixed-point algorithm.

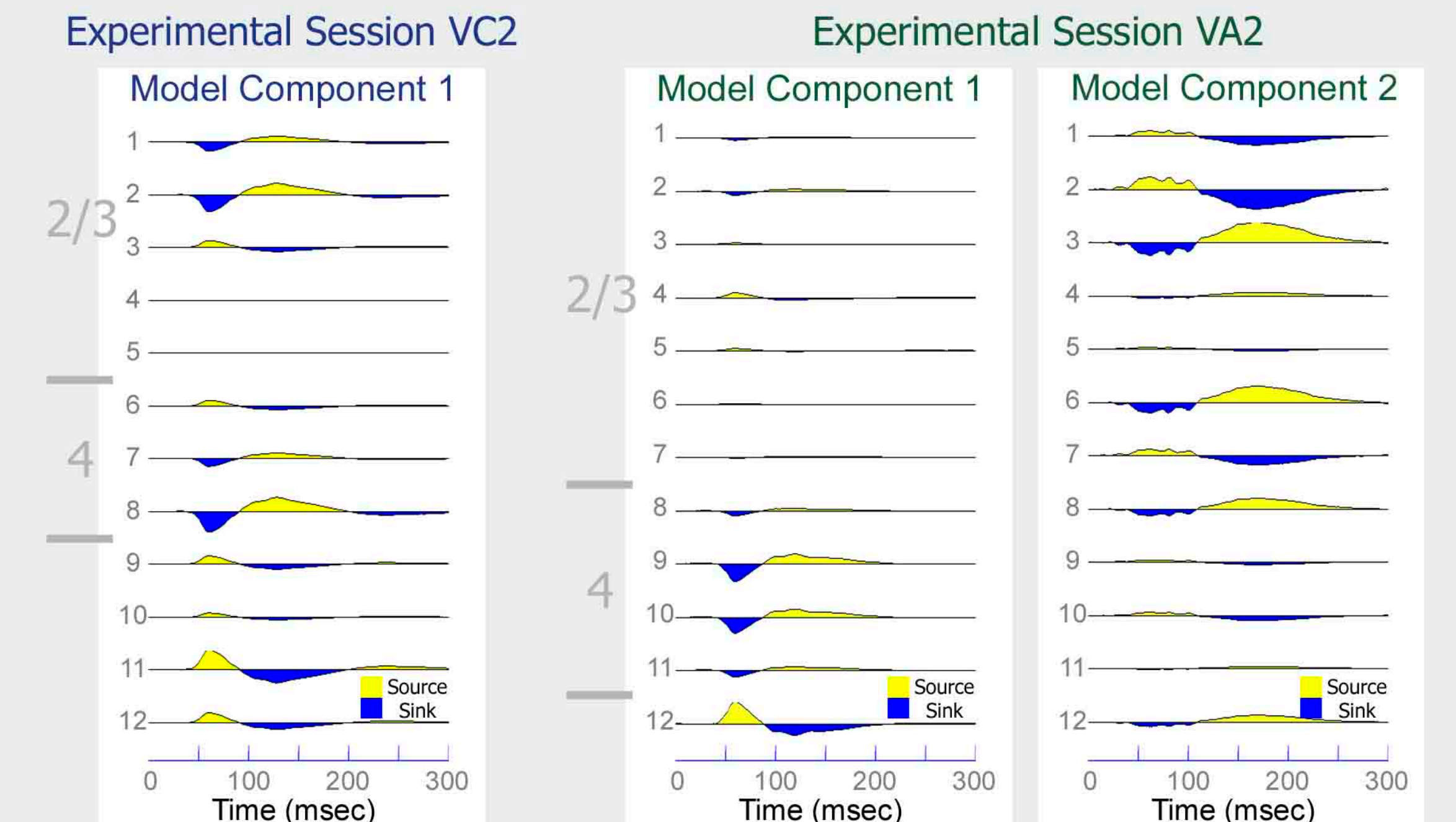
## Experimental Paradigm



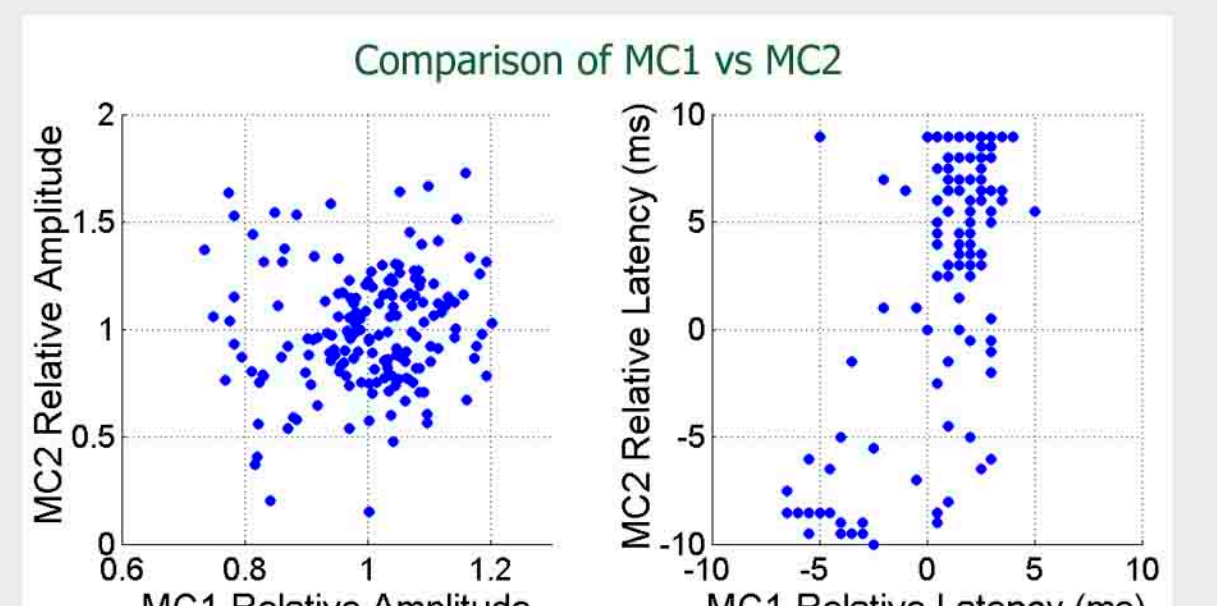
<sup>1</sup>Current source density (CSD) indicates the direction and magnitude of transmembrane current flow, which is responsible for generating field potential (FP) and sometimes MUA. The CSD is approximated as the second spatial derivative of the FP.

## Modeling Results

The mcERP model was applied to single-trial FP data resulting in estimates of component waveshapes and their associated spatial locations and single-trial amplitudes and latencies. Below are CSD maps of the model components.



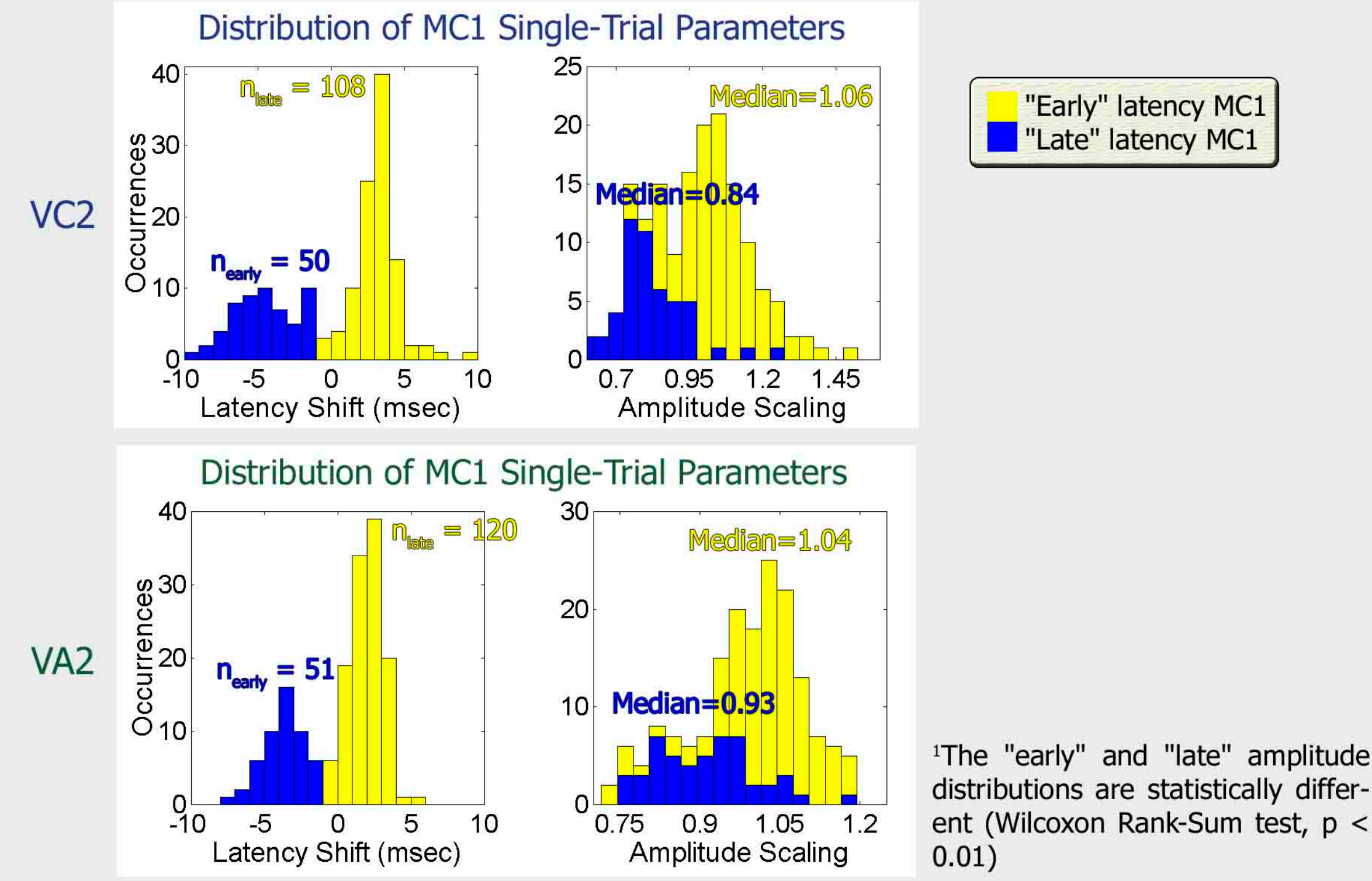
mcERP can isolate linearly coupled sources if their electrical activities have differing waveshapes. Modeling of VC2 generates a single, distributed component describing granular and supragranular activation suggesting resolution of activity related to layer 4C populations and their supragranular axonal projections.<sup>1</sup> Conversely, modeling of VA2 illustrates two distinct components, where VA2 Model Component 1 (MC1) may represent layer 4C activation and VA2 MC2 may be post-synaptic activity in the supragranular layers driven by the layer 4C activation. This hypothesis can be tested by examining co-variance in trial-to-trial variability between these components (right).



<sup>1</sup>Tenckle et al. [1993] showed that thalamic axons may contribute to CSD activity in layer 4 and below. Similarly, axons may be contributing to the activity measured in the supragranular layers.

## Bimodal Activation of Layer 4C

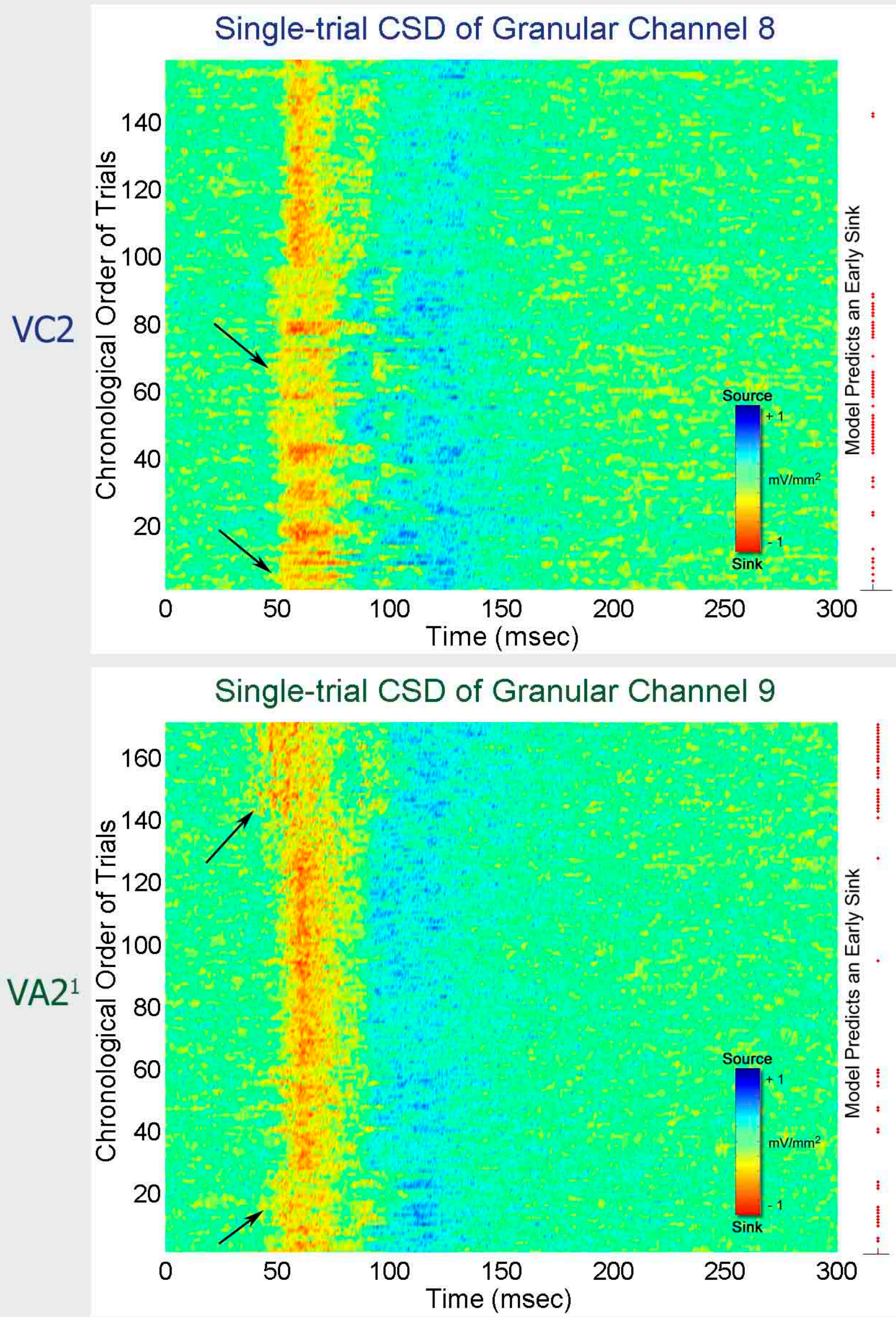
Since the model permits trial-to-trial latency and amplitude variability, we can examine these dynamics to characterize activation patterns in different laminae. The initial activation of layer 4C illustrates a bimodal latency distribution in both experimental sessions. Furthermore, "early" activation is associated with smaller amplitude responses, and "late" activation is associated with larger responses.<sup>1</sup> Note that the overall amplitude variability is small in both cases.



<sup>1</sup>The "early" and "late" amplitude distributions are statistically different (Wilcoxon Rank-Sum test,  $p < 0.01$ )

## Verifying the Model in Layer 4C

To verify the modeling results, we examined single-trial data from each session. The plots show trial-to-trial variability in layer 4 activation and illustrate that the response in some trials occurs early (arrows). The red markers to the right indicate trials in which the modeled response had an "early" relative latency.



<sup>1</sup>To further verify modeling results, cross correlation between the average response of Channel 9 in VA2 (windowed between 25 and 95 ms) and single-trial data was also utilized to estimate the latency of this initial sink. The resulting distribution illustrated bimodality. These results are not shown here.

## Discussion

The mcERP model permits examination of system dynamics by estimating single-trial responses to a stimulus. The data presented illustrated both session-to-session and trial-to-trial variability, which are important in interpreting the response to a particular sensory stimulus. First, session-to-session variability may manifest from variations in multielectrode positioning with respect to the sources and sinks of activity. The modeling of VC2 shows that we must be open to the idea of distributed components and further that field potential activity may be generated by an ensemble of neuronal elements instead of a single cell population. Second, characterization of the trial-to-trial variability suggests that V1 may have two transmission states. mcERP model results and single-trial data illustrate that these two states occur in groups of trials and are rarely interspersed. Given this evidence, these transmission states may be related to slow drifts in eye position across the fixation window or global shifts of attention. Each of these possibilities will be explored to better understand the transmission patterns through V1. Finally, these results indicate that we can estimate single-trial evoked responses, which can be subtracted from actual data to examine stimulus-induced modulation of ongoing EEG rhythms.

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Please visit 506.4 for information on the validation of mcERP.